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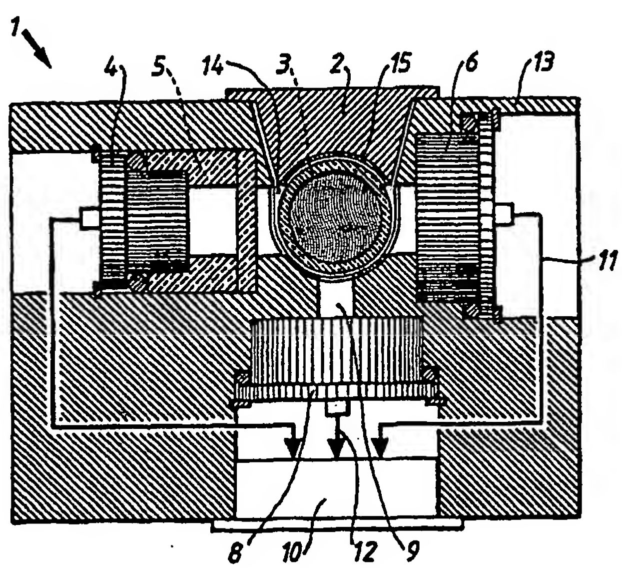
(54) Title: METHOD AND DEVICE FOR MEASURING BLOOD PARAMETERS



(57) Abstract

Method and device for providing a signal. The signal is proportional to total hemoglobin or a concentration of red cells in flowing blood. Blood is passed through a cuvette and exposed to light passing along a transmission path through the blood in the cuvette. A transmitted signal sensor and a scattered signal sensor are arranged at a mutual angle of 90°. The transmitted signal sensor receives light passing along the transmission path straight through the blood in the cuvette. The scattered light sensor receives light scattered at 90° in relation to the transmission path. The ratio signal is the ratio between the scattered signal and the transmitted signal. To decrease the crosstalk between the signals, the area surrounding the cuvette is painted with light absorbing colour.

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TITLE: METHOD AND DEVICE FOR MEASURING BLOOD PARAMETERS

AREA OF INVENTION

The present invention relates to a method and a device for measuring blood parameters and more specifically for providing an optical signal proportional to total hematocrit or a concentration of red cells in blood. More in details, the invention relates to continuous measurement of the vascular blood volume during dialysis.

PRIOR ART

Many optical sensors for measurement on whole blood are designed for measuring the light transmission or reflection properties of blood, see for example WO 94/08237, WO 95/04266, EP-467804, EP-800074, EP-818682 and US 5351686.

These measurements often fails to take into account the scattering properties of blood. The omission of this information results in data distorted by the light scattering of blood and consequently by properties like the size, shape and orientation of the cells. The two latter properties are of particular significance when conducting measurements on flowing blood.

A more extensive measurement procedure is required in order to obtain results with minimal contribution of the scattering properties, like an assessment of the angular distribution of the light transmission, as described in e.g US 5,601,080, by recording the change in transmission at more than one wavelength, as described in e.g. US 4,810,090, or at varying sample thickness.

Another drawback with previously known measurement methods for deducing the hematocrit or hemoglobin is that the

transmission signal has an exponential relationship with hematocrit or total hemoglobin. This means that the accuracy of the derived results are highly dependent on the quality of the calibration routine used. Moreover, the relationship is dependent on the oxygen saturation level of the blood and the osmolarity. Finally, and of great importance, the relationship is dependent on the flow rate of the blood in a complex manner, making it difficult to correct for the flow rate.

Patients suffering from end stage renal decease are regularly exposed to dialysis, essentially for removing waste products from the blood, balancing electrolytes, supplying buffer and removing excess water. During the removal of excess water, such water is removed from the contents of the blood vessels, resulting in a decreased blood volume. The removal is balanced by vascular refilling from the surrounding tissue. However, if the blood volume is caused to decrease too much and too fast, the patient may suffer various symptomatic complications, like hypotension, cramps, nausea and headache.

By measuring the concentration of red blood cells in the blood, a change of the blood volume can be estimated and an excessive reduction of the blood volume may be detected.

SUMMARY OF THE INVENTION

An object of the invention is to provide an optical measurement method and device for measurement on whole blood, which are robust and rugged and provide an output signal which inherently is essentially proportional to the concentration of red blood cells.

Another object of the invention is to provide an optical measurement method and device suitable for measurement on flowing whole blood.

A further object of the invention is to provide an optical measurement method and device having an increased sensitivity.

A still further object of the invention is to provide an optical measurement method and device suitable for use as a blood volume sensor during dialysis.

According to the invention, it is observed that both the transmitted signal as well as the side scattered signal have

information essential for the evaluation of the red cell concentration in blood. Both signals decrease at increasing concentration and the relationships are non-linear. The signals are dependent on oxygen saturation level, osmolarity and have a complex dependency on blood flow rate.

However, it has been found, according to the invention, that the ratio between the perpendicular scattered signal and the transmitted signal is essentially proportional to the red cell concentration, i.e. there is a linear relationship between the ratio signal and the red cell concentration. The ratio signal has, moreover, merely a small dependency on oxygen saturation level, osmolarity and blood flow rate.

Thus, according to the invention, there is provided a method and device for providing a signal proportional to a concentration of red cells in blood, total hemoglobin or hematocrit, comprising: flowing blood through a cuvette; exposing the flowing blood to light passing along a straight transmission path through the blood in the cuvette; measuring light transmitted along said transmission path to obtain a transmitted signal; measuring scattered light at an angle perpendicular to said transmission path to obtain a scattered signal; and forming a ratio signal which is the ratio between the scattered signal and the transmitted signal. The sensitivity may be increased by adapting light absorbing material at areas surrounding the cuvette or parts thereof.

DETAILED DESCRIPTION OF DRAWINGS

Further objects, features and advantages of the invention appear from the ensuing description of an embodiment of the invention with reference to the drawings.

Fig. 1 is a schematic cross sectional view of an embodiment of the invention.

Fig. 2 is a diagram showing the scattered and transmitted signals versus total hemoglobin recorded by the embodiment of Fig. 1.

Fig. 3 is a diagram showing the ratio signal between the scattered signal and transmitted signal versus total hemoglobin.

Fig. 4 is a diagram showing the relationship between the ratio signal recorded by the embodiment of Fig. 1 versus hematocrit as measured by a reference instrument.

Fig. 5 is a diagram showing the relative change of the signals of the embodiment according to Fig. 1, with and without light absorbtion painting.

Fig. 6 is a diagram showing the relative change of the transmitted signal, scattered signal and ratio signal versus blood oxygenation.

Fig. 7 is a diagram showing the relative change of the transmitted signal, scattered signal and ratio signal versus osmolarity represented by sodium chloride concentration.

Fig. 8a, 8b and 8c are diagrams showing the relative change of the transmitted signal, scattered signal and ratio signal versus blood flow rate.

DETAILED DESCRIPTION OF AN EMBODIMENT

Fig. 1 discloses a schematic cross-sectional view of a first embodiment of the invention. The blood sensor 1 comprises a cavity 14 closed by a lid 2. The cavity is adapted to receive a flow cuvette 3, which is shown in place in Fig. 1.

The flow cuvette can be inserted and removed from the cavity 14 through the opening provided by said lid 2. The flow cuvette may have a circular cross-section as shown in the drawings or may have any desired cross-section, such as rectangular. The cuvette is preferably made of hard transparent plastics material and is designed to have the same cross-sectional area over the entire length.

The flow cuvette may be included in a tube set for an extracorporeal blood circuit such as a tube set intended for hemodialysis, hemofiltration, hemodiafiltration, plasmapheresis, blood component separation, oxygenation or similar treatments. Preferably, the tube set and the cuvette comprises whole blood from a mammal having a red blood cell concentration to be measured by the blood sensor according to the invention.

The blood sensor 1 further comprises a light emitting diode LED 4 mounted in a housing 5 for emitting light at a

predetermined cone angle of approximately 120°. LED 4 emits light of a predetermined wavelength, which preferably is at an isobestic point for which the influence of oxygen saturation is at minimum. The wavelength preferred according to the invention is 805 nm. Alternative wavelength may be 548 and 586 nm.

Opposite to the LED 4 there is arranged a first photo diode 6, called the transmitted light diode below, for receiveing light from the LED 4 transmitted through the flow cuvette essentially along a diameter of the cuvette, extending from the LED towards the diode 6. Transmitted light diode 6 provides a signal indicative of the transmitted light intensity. The diode 6 is arranged to receive collimated light passing through a straight transmission path 7, which extends from the LED 4 towards the diode 6.

Perpendicular to the transmission path 7, there is arranged a second photo diode 8, called the scattered light diode below, for receiving light emitted by LED 4 and side scattered essentially perpendicular to the transmission path by the contents of the flow cuvette. Scattered light diode 8 receives light through an opening 9 to minimise any undesired direct light from the LED 4. Scattered light diode 8 emits a signal indicative of the side scattered light scattered over 90°.

The signals emitted by transmitted light diode 6 and scattered light diode 8 are fed to a computing unit 10 via wires 11 and 12. The computing unit may be a central computing unit arranged in the machine, in which the blood sensor 1 is connected, or may be arranged in the blood sensor proper as indicated in Fig. 1.

The computing unit is arranged to calculate a ratio signal by dividing the scattered light signal provided by the scattered light diode 8 and the transmitted light signal provided by the transmitted light diode 6 to provide an optical ratio signal according to the invention. The computing unit may also provide drive signals to the LED 4 to have full control of the operation of the blood sensor. The drive signals may be pulsed signals to reduce the influence of background light on

the recorded scattered and transmitted light signals provided by the light diodes 8 and 6, respectively.

The different components of the blood sensor 1 are mounted in a housing 13 provided with openings and recesses and shoulders as required to provide support for the LED 4 and the photo diodes 6 and 8. As shown in Fig. 1, these components may be mounted by means of O-rings.

The interior surfaces of the cavity 14 may be covered by a light absorbing material like black painting 15 as shown in Fig. 1, in order to reduce the risk that the transmitted and scattered light signals are distorted by reflections in the cavity.

The signals emitted by the transmitted light diode 6 and the scattered light diode 8 are shown in Fig. 2 versus total hemoglobin in gram/litre for bovine blood at a flow rate of 300 ml/min. As expected they both have a typical exponential decay with increasing total hemoglobine, which substantially corresponds to the concentration of red blood cells.

As shown in Fig. 3, the ratio signal has, however, a substantially linear relationship with total hemglobine. This linear relationship is a highly desired property, since it provides a robust signal to be used for measuring total hemoglobin or concentration of red blood cells.

Fig. 4 shows the ratio signal compared with a signal from an accurate reference hematocrit sensor, provided by In-Line Diagnostics Corporation under the trademark Crit-Line. As clearly appears from Fig. 4, the ratio signal according to the invention is substantially proportional to the hematocrit as measured by the reference instrument, with a correlation coefficient close to unity (0.991). The measurements were performed with bovine blood at a blood flow rate of 300 ml/min.

Fig. 5 shows the ratio signal according to the present invention with reflecting cavity surfaces and with absorbing cavity surfaces, the surfaces being painted with light absorbing colour or coating. As clearly appears from Fig. 5, the ratio signal has a larger slope when the reflections in the cavity has been eliminated. Moreover, the linearity at high total hemoglobin is better with absorbing surfaces. The reason

for this is probably that the transmitted signal is very low at high total hemoglobin concentrations and that background light is reflected to the transmitted light diode 6 and disturbes the correct signal. Also the scattered light signal might be corrupted by reflections.

Fig. 6 shows the relative change of the transmitted signal, the side scattered signal and the ratio signal when the oxygenation level of the blood is increased from 50% to 95%. Both the transmitted and the scattered signals have a high relative change, while the ratio signal has a low dependency, making it ideal for measurement at varying oxygenation levels. The indicated change takes place in spite of the fact that the peak wavelength of the light used is centred at the isobestic point, here 805 nm, for which the changes due to the oxygenation level are minimal.

Fig. 7 discloses the relative change of the transmitted signal, the side scattered signal and the ratio signal versus different sodium chloride concentrations, around the physiological level of 0.90%, which is the reference point for the diagram. The diagram suggests the dependency of the signals to different osmolarities of the fluid. The osmolarity affects the size and shape of the red blood cells. As appears from Fig. 7, the ratio signal varies less than the other signals at varying osmolarity.

Finally, Figs. 8a, 8b and 8c indicates the relative change of the three signals for different flow rates between 50 ml/min to 450 ml/min, which are the flow rates commonly used during extracorporeal blood treatment, and at different total hemoglobin. The flow rate is expected to influence upon the red blood cells, mainly on the shape and alinement of the cells.

Significant influences of the flow rate can be observed on the measured signals, which in turn depend on the concentration of red blood cells, represented by the total concentration of hemoglobin. The ratio signal is less influenced by the flow rate and not significantly affected by the total hemoglobin.

The benefical linearity of the ratio signal with total hemoglobin has been found for light scattered substantially 90° in relation to the transmission signal. Since both signals are

exponential, the ratio is linear only if the exponents are substantially the same. It has been found, according to the invention, that this happens only when the light is scattered over substantially 90°. However, substantially the same effect appears at light scattered between 70° and 110°, more specifically between 80° and 100°.

The optical blood sensor described above, has been demonstrated to be useful for providing a ratio signal which is linearly related to hematocrit, total hemoglobin or concentration of red blood cells. The blood sensor may be used in connection with extracorporeal blood treatment to detect concentration of blood or measure blood volume during for example hemodialysis.

The blood concentration signal obtained from the blood sensor is robust and only slightly affected by oxygenation level, osmolarity and blood flow rate. Moreover, the accuracy is relatively high. These properties makes the blood sensor ideal for use as a feedback control instrument for controlling the blood volume by feed back during treatment.

The blood sensor may alternatively be used as an instrument for alerting the dialysis care personell about an imminent hazardous condition, like hypotension.

The invention has been described above with reference to an embodiment shown on the drawings, but a skilled person reading the present specification may further amend and adapt the device as required to different areas of application. Other combinations than those suggested above are feasable. Such equivalent constructions are intended to be within the scope of the invention as indicated in the patent claims below.

PATENT CLAIMS

1. A method for providing a signal proportional to a concentration of red cells in blood, comprising:

flowing blood through a cuvette;

exposing the flowing blood to light passing along a straight transmission path through the blood in the cuvette;

measuring light transmitted along said transmission path to obtain a transmitted signal;

measuring scattered light at an angle to said transmission path to obtain a scattered signal;

characterised by

forming a ratio signal which is the ratio between the scattered signal and the transmitted signal, in which said angle is substantially 90° in relation to the transmission path.

2. A method as claimed in claim 1, **characterised** in that said angle is between 70° and 110°, or preferably between 80° and 100°.

3. A method as claimed in claim 1 or 2, further comprising

exposing the flowing blood for light by means of a light emitting member;

measuring the transmitted light by means of a first light sensitive member;

measuring the scattered light by means of a second light sensitive member;

characterised in

increasing the sensitivity of the ratio signal by adapting light absorbing material at areas surrounding the cuvette or parts thereof.

4. A method as claimed in claim 3, **characterised** in that the light emitting member emits light with a restricted emission angle.

5. A method as claimed in claim 3 or 4, **characterized** in that said light emitting member is activated in a pulsed mode.

6. A device intended for performing the method of any one of the preceding claims, for providing a signal proportional to a concentration of red cells in blood,
comprising:

a cuvette comprising flowing blood;

a light emitting member for exposing the flowing blood for light passing along a straight transmission path through the blood in the cuvette;

a first light sensitive member for measuring light passing along said transmission path to obtain a transmitted signal;

a second light sensitive member for measuring scattered light at an angle to the transmission path to obtain a scattered signal;

characterised by

calculation means for forming a ratio signal which is the ratio between the scattered signal and the transmitted signal, in which said angle is substantially 90° in relation to the transmission path.

7. A device as claimed in claim 6, **characterised** in that said second light sensitive member is arranged at an angle of between 70° and 110°, or preferably between 80° and 100°.

8. A device as claimed in claim 6 or 7, **characterised** by light absorbing material arranged at areas surrounding the cuvette or parts thereof.

9. A device as claimed in claim 8, **characterised** in that the light emitting member has a restricted emission angle.

10. A device as claimed in any one of claims 6 to 9, **characterised** in that the light emitting member is driven in a pulsed mode.

Fig. 1

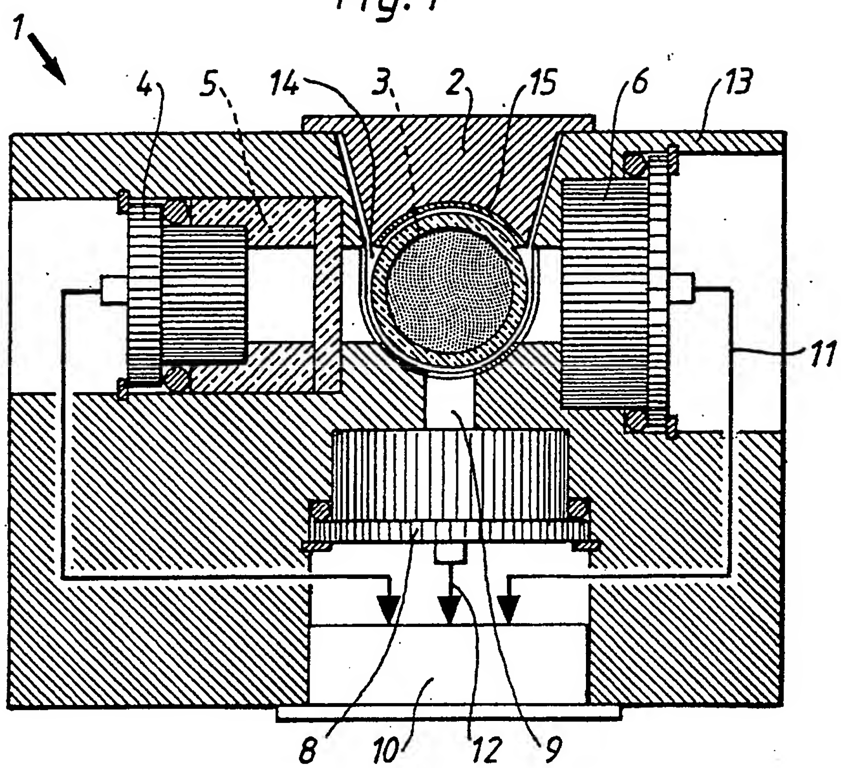

1
4
5
14
3
2
15
6
13
11
8
10
12
9

Fig. 2

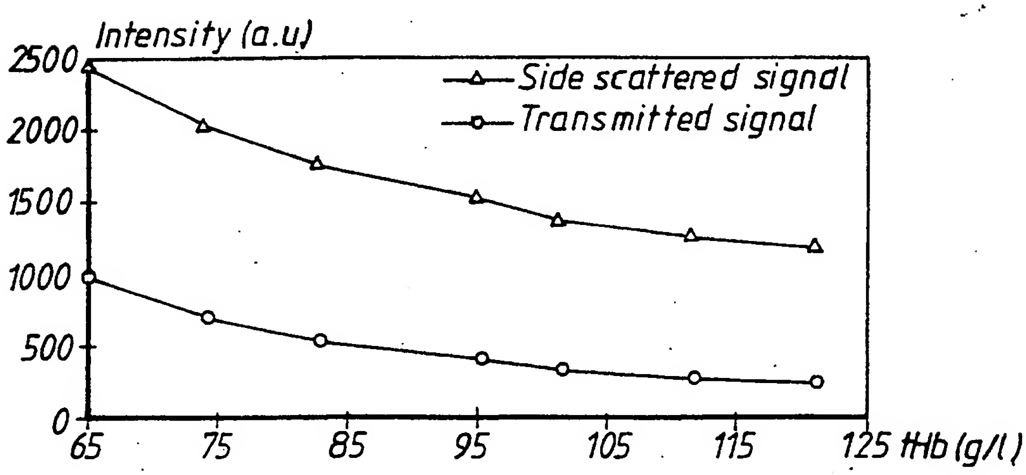

Intensity (a.u)
2500
2000
1500
1000
500
0
Side scattered signal
Transmitted signal
65
75
85
95
105
115
125 tHb (g/l)

Fig. 3

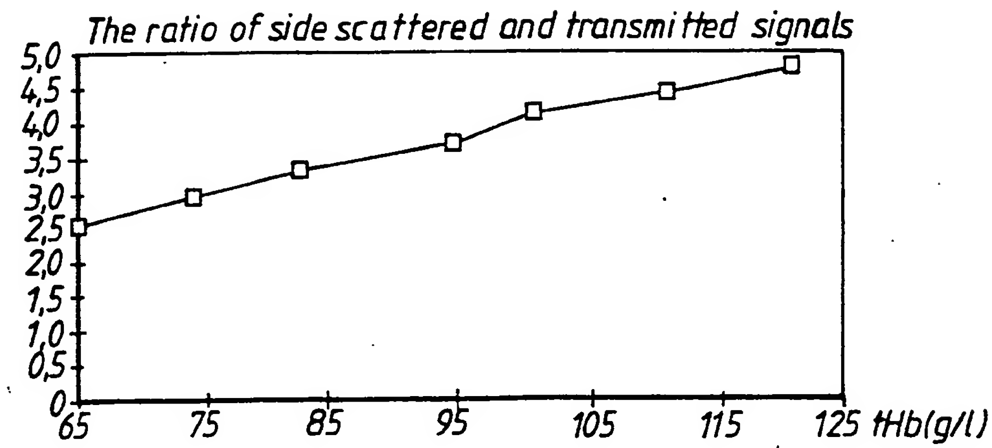


Fig. 5

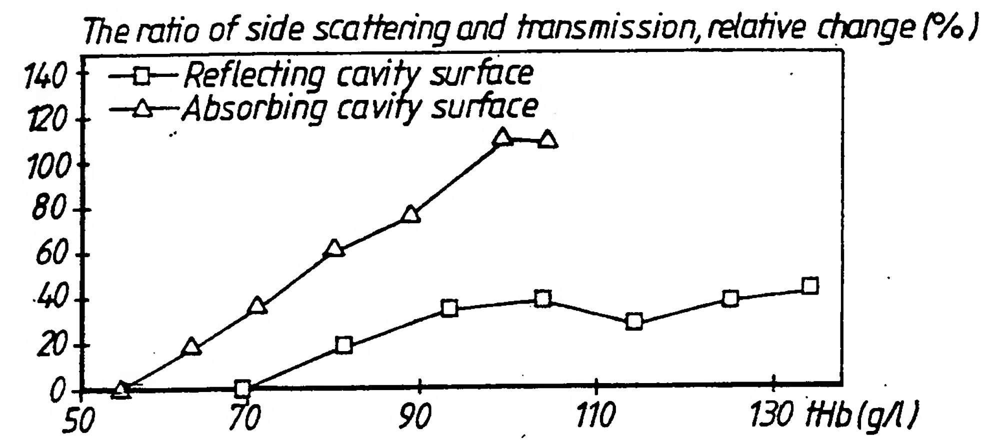


Fig. 4

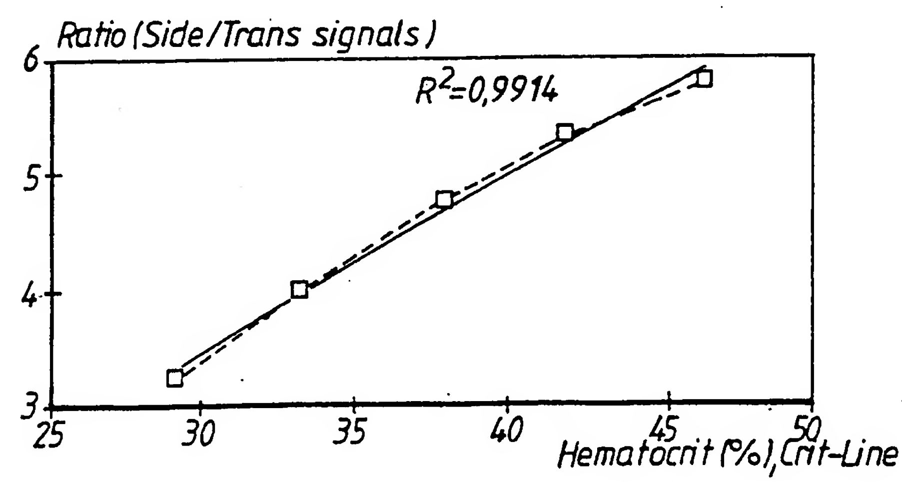


Fig.6

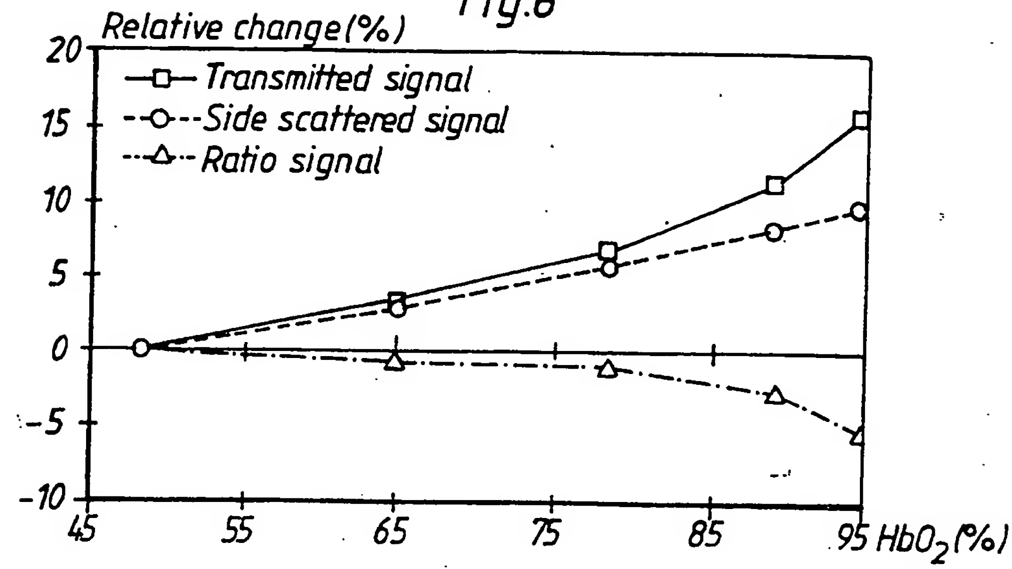


Fig.7

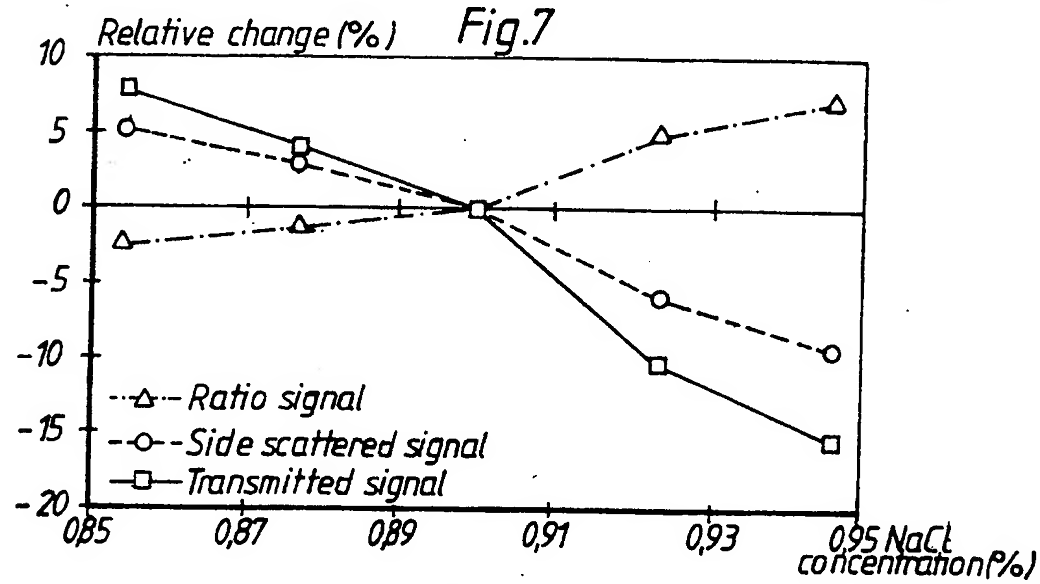


Fig.8 a

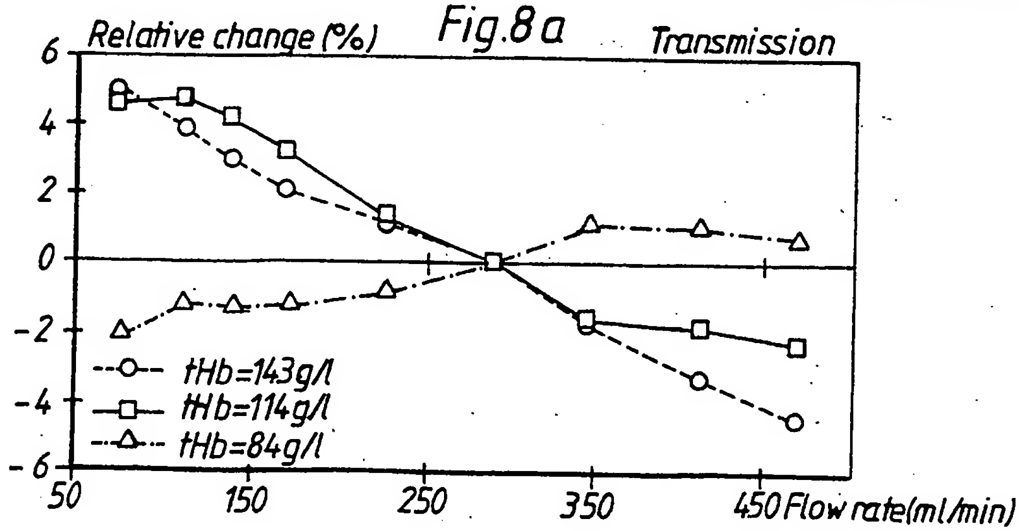
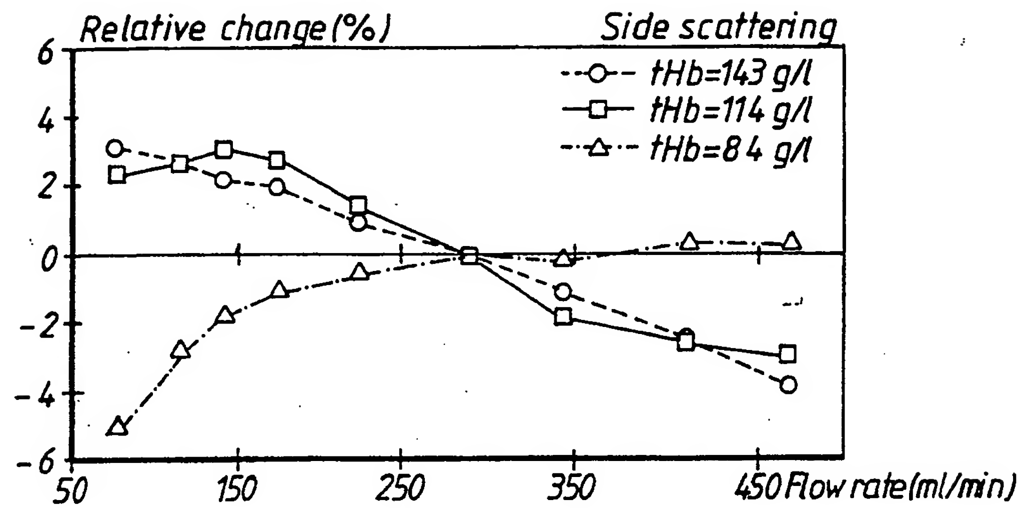


Fig. 8b


Relative change (%)
Side scattering
--○-- tHb=143 g/l
—□— tHb=114 g/l
-·-△-·- tHb=84 g/l
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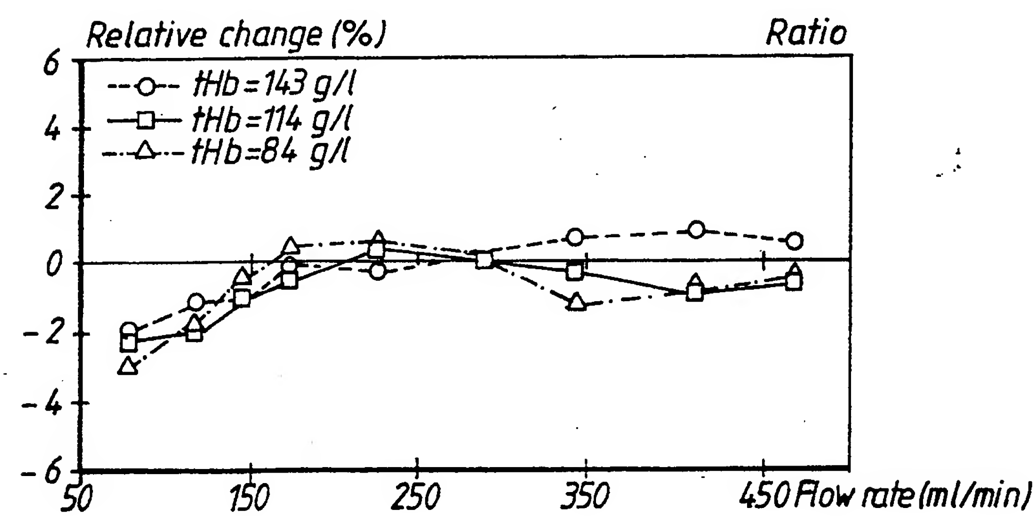
4
2
0
-2
-4
-6
50
150
250
350
450
Flow rate (ml/min)

Fig. 8c


Relative change (%)
Ratio
--○-- tHb=143 g/l
—□— tHb=114 g/l
-·-△-·- tHb=84 g/l
6
4
2
0
-2
-4
-6
50
150
250
350
450
Flow rate (ml/min)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 99/02219

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: G01N 21/53, G01N 33/49

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4810090 A (TERRY D. BOUCHER ET AL), 7 March 1989 (07.03.89), the abstract; column 1, line 43; column 7, lines 48-56 and the claims --	1-10
A	EP 0720013 A2 (CORETECH MEDICAL TECHNOLOGIES CORPORATION), 3 July 1996 (03.07.96), page 4, lines 34-35, 53-56; page 6, lines 28-29, 38-48 and claim 8 -- --------	1-10

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Date of the actual completion of the international search	Date of mailing of the international search report
14 March 2000	31-03-2000

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.
PCT/SE 99/02219

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		AU 2108488 A	02/03/89
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		IT 8867772 D	00/00/00
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EP 0720013 A2	03/07/96	US 5601080 A	11/02/97